

Amendments to the Specification:

Please replace the title at page 1, line 1 with the following title:

-- SAMPLING METHOD ~~AND APPARATUS~~ FOR AMPLIFICATION REACTION ANALYSIS --

On page 47, please replace the Abstract with the following amended Abstract:

-- The invention provides sampling methods that permit the quantitative analysis of nucleic acid amplification reactions. ~~Quantitative information garnered during an amplification regimen permits the development of a detailed amplification profile that in turn permits the reliable determination of original template abundance.~~ The methods disclosed are particularly useful for permit quantitative expression analysis of multiple genes or transcription units, both in the same amplification reaction and in multiple amplification reactions. In one aspect, the methods disclosed include, briefly, dispensing or withdrawing an aliquot from a reaction mixture at plural stages of an amplification regimen, separating and detecting nucleic acids in the aliquot, determining the quantity of a plurality of separated nucleic acid species in the aliquot, and for each separated nucleic acid species from each stage, correlating the quantity of the species with the stage at which the aliquot comprising the species was dispensed, thereby generating a profile of the amplification. --

The following Listing of the Claims will replace all prior versions and all prior listings of the claims in the present application:

Listing of The Claims:

1. (Currently Amended) A method of analyzing a nucleic acid amplification, the method comprising:

providing a nucleic acid amplification reaction mixture comprising a plurality of different amplification templates;

subjecting said reaction mixture to an amplification regimen;

dispensing or withdrawing an aliquot from said reaction mixture at plural stages during said amplification regimen;

separating and detecting nucleic acids in said aliquot;

determining the quantity of a plurality of separated nucleic acid species in said aliquot;

and

for each said separated nucleic acid species from each said stage, correlating the quantity of said species with the stage at which said aliquot comprising said species was dispensed, wherein said correlating generates an amplification profile of said nucleic acid amplification.

2. (Original) The method of claim 1 wherein said plurality of different amplification templates comprises at least three different amplification templates.

3. (Original) The method of claim 1 wherein said plurality of different amplification templates comprises at least five different amplification templates.

4. (Original) The method of claim 1 wherein said plurality of different amplification templates comprises at least ten different amplification templates.

5. (Original) The method of claim 1 wherein said plurality of different amplification templates comprises at least 20 different amplification templates.

6. (Original) The method of claim 1 wherein said plurality of different amplification templates comprises at least 50 different amplification templates.

7. (Original) The method of claim 1 wherein said plurality of different amplification templates comprises at least 100 different amplification templates.

8. (Original) The method of claim 1 wherein said plurality of different amplification templates

comprises at least 200 different amplification templates.

9. (Original) The method of claim 1 wherein a plurality of amplification reaction mixtures is subjected to said method.

10. (Original) The method of claim 9 wherein said plurality of amplification reaction mixtures is subjected to said method simultaneously.

11. (Original) The method of claim 1 wherein said method generates an amplification profile for a plurality of amplified nucleic acid species.

12. (Original) The method of claim 1 wherein said amplification profile provides quantitative information regarding the abundance of a nucleic acid species present in said nucleic acid amplification reaction mixture at the start of said amplification regimen.

13. (Original) The method of claim 1 wherein said amplification profile is a transcriptional profile.

14. (Original) The method of claim 1 wherein said nucleic acid amplification regimen comprises thermal cycling.

15. (Original) The method of claim 1 wherein said nucleic acid amplification regimen comprises isothermal cycling.

16. (Original) The method of claim 1 wherein said nucleic acid amplification regimen comprises PCR.

17. (Original) The method of claim 1 wherein said nucleic acid amplification regimen comprises a method selected from the group consisting of ligase-mediated amplification, NASBA, and rolling circle amplification.

18. (Original) The method of claim 1 wherein said aliquot is dispensed into a receptacle having a plurality of aliquot-receiving sites.

19. (Original) The method of claim 18 wherein said receptacle is a multiwell plate.

20. (Original) The method of claim 1 wherein said aliquot is dispensed into or onto a receptacle capable of holding a plurality of aliquots without mixing among said aliquots.

21. (Original) The method of claim 18 wherein said receptacle comprises a plurality of CE capillaries.

22. (Original) The method of claim 1 wherein said amplification regimen is cyclic.

23. (Original) The method of claim 22 wherein said dispensing or withdrawing is performed

after each of a plurality of cycles.

24. (Original) The method of claim 22 wherein said dispensing or withdrawing is performed after every cycle in said regimen.

25. (Original) The method of claim 1 wherein said separating comprises electrophoresis.

26. (Original) The method of claim 1 wherein said separating comprises capillary electrophoresis.

27. (Original) The method of claim 1 wherein said separating comprises liquid chromatography.

28. (Original) The method of claim 18 wherein said detecting comprises detection of one or more fluorescent labels.

29. (Original) The method of claim 18 wherein said detecting comprises mass spectrometry.

30. (Original) The method of claim 1 wherein said amplification regimen is performed in a container, and wherein said aliquot dispensing is performed by withdrawing said aliquot from said container.

31. (Original) The method of claim 19 wherein said container is a well or a test tube.

32. (Original) The method of claim 1 wherein said amplification regimen is performed in a container, and wherein said dispensing is performed by extruding said aliquot from said container.

33. (Original) The method of claim 32 wherein said amplification regimen is performed in a container open at one or both ends.

34. (Original) The method of claim 32 wherein said container is a capillary tube.

35. (Original) A method of analyzing the expression of a plurality of RNA transcripts between first and second gene expressing entities, said method comprising

providing a first nucleic acid amplification reaction mixture, said mixture comprising a plurality of different amplification templates, wherein said amplification templates comprise reverse transcription products from a plurality of RNA transcripts from a first gene expressing entity;

providing a second nucleic acid amplification reaction mixture, said mixture comprising a plurality of different amplification templates, wherein said amplification templates comprise reverse transcription products from a plurality of RNA transcripts from a second gene expressing entity;

subjecting said reaction mixtures to an amplification regimen;  
dispensing or withdrawing an aliquot from said first and said second reaction mixtures at plural stages during said amplification regimen;  
separating and detecting nucleic acids in said aliquot;  
determining the quantity of a plurality of separated nucleic acid species in said aliquot;  
for each said separated nucleic acid species from each said stage, correlating the quantity of said species with the stage at which said aliquot comprising said species was dispensed, thereby generating a transcriptional profile of said plurality of RNA transcripts expressed by said first and said second gene expressing entities; and

comparing said transcriptional profile from said first gene expressing entity with said transcriptional profile from said second gene expressing entity.

36. (Original) The method of claim 35 wherein said plurality of RNA transcripts comprises at least three different RNA transcripts.

37. (Original) The method of claim 35 wherein said plurality of RNA transcripts comprises at least five different RNA transcripts.

38. (Original) The method of claim 35 wherein said plurality of RNA transcripts comprises at least ten different RNA transcripts.

39. (Original) The method of claim 35 wherein said plurality of RNA transcripts comprises at least 20 different RNA transcripts.

40. (Original) The method of claim 35 wherein said plurality of RNA transcripts comprises at least 50 different RNA transcripts.

41. (Original) The method of claim 35 wherein said plurality of RNA transcripts comprises at least 100 different RNA transcripts.

42. (Original) The method of claim 35 wherein said plurality of RNA transcripts comprises at least 200 different RNA transcripts.

43. (Original) The method of claim 35 wherein said amplification regimen is cyclic.

44. (Original) The method of claim 43 wherein said nucleic acid amplification regimen comprises thermal cycling.

45. (Original) The method of claim 43 wherein said nucleic acid amplification regimen comprises isothermal cycling.

46. (Original) The method of claim 43 wherein said nucleic acid amplification regimen comprises PCR.
47. (Currently Amended) The method of claim 35 wherein said nucleic acid amplification regimen comprises ligase-mediated amplification, NASBA, ~~and~~ or rolling circle amplification.
48. (Original) The method of claim 35 wherein said aliquot is dispensed into a receptacle having a plurality of aliquot-receiving sites.
49. (Original) The method of claim 48 wherein said receptacle is a multiwell plate.
50. (Original) The method of claim 48 wherein said receptacle comprises a plurality of CE capillaries.
51. (Original) The method of claim 43 wherein said dispensing or withdrawing is performed after a plurality of cycles.
52. (Original) The method of claim 43 wherein said dispensing or withdrawing is performed after every cycle in said regimen.
53. (Original) The method of claim 35 wherein said separating comprises electrophoresis.
54. (Original) The method of claim 35 wherein said separating comprises capillary electrophoresis.
55. (Original) The method of claim 35 wherein said separating comprises liquid chromatography.
56. (Original) The method of claim 35 wherein said detecting comprises detection of one or more fluorescent labels.
57. (Original) The method of claim 35 wherein said detecting comprises mass spectrometry.
58. (Original) The method of claim 35 wherein said amplification regimen is performed in a container, and wherein said aliquot dispensing is performed by withdrawing said sample from said container.
59. (Original) The method of claim 58 wherein said container is a well or a test tube.
60. (Original) The method of claim 35 wherein said amplification regimen is performed in a container, and wherein said dispensing is performed by extruding said aliquot from said container.
61. (Original) The method of claim 60 wherein said container is a capillary tube.
62. (Original) A method of monitoring the amplification of a nucleic acid sequence, the method comprising:

providing a nucleic acid amplification reaction mixture comprising a template of said nucleic acid sequence;

performing an amplification regimen on the mixture;

automatically dispensing an aliquot of said reaction mixture at plural stage intervals throughout the amplification regimen;

separating and detecting the nucleic acid species in said aliquot; and,

for respective ones of plural separated species, determining the quantity of separated nucleic acid in said aliquot.

63. (Currently Amended) A method of determining the transcription profile of a nucleic acid sequence, the method comprising:

providing a nucleic acid amplification reaction mixture;

performing an amplification regimen on the mixture;

dispensing an aliquot of said reaction mixture at plural stage intervals throughout the amplification regimen;

separating and detecting the nucleic acid species in said aliquot; and,

for respective ones of plural separated species, determining the quantity of separated nucleic acid in said aliquot; and

determining the whereby a transcription profile of said nucleic acid sequence transcripts in a nucleic acid sample which correspond to respective ones of said plural separated species is determined.